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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/777,211

02/13/2004

Markku Anttila

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2487

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EXAMINER

GEMBEH, SHIRLEY V

ART UNIT

PAPER NUMBER

1628

MAIL DATE

DELIVERY MODE

01/19/2011

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/777,211	Applicant(s) ANTTILA, MARKKU	
	Examiner SHIRLEY V. GEMBEH	Art Unit 1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 November 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-5 and 7-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-5 and 7-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/29/10 has been entered.

2. The response filed on **11/29/10** presents remarks and arguments to the office action mailed on **6/4/10**. Applicant's request for reconsideration of the rejection of claims in the last office action has been considered.

Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 1, 3-5, 7-20 and 21-24 are pending in this action. Claims 1, 3-5 and 7-8 are currently amended and claims 21-24 are newly added.

New Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 7, 10-11 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation “....said foodstuff is being taken shortly before.....shortly after is vague and indefinite which is a relative term. Thus the term shortly before or shortly after does not provide a standard for ascertaining the requisite degree, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention, because one of skill will not be able to determine what is meant by the term shortly before or shortly after.

New Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

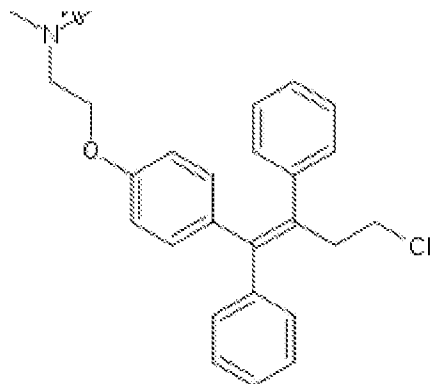
Claims 1, 3-5, 7, 10-11, 14 and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over DEGregorio et al. (US 5,750,576) in view of Anttila (1997) and further in view of Guidance for Industry (2002, already of record).

DEGregorio et al. teaches treating osteoporosis by administering ospemifene (see abstract), as required by instant claims 1-2, 7, 10-11, 14 in a pharmaceutically acceptable salt is obvious since it is in a pharmaceutical composition. DEGregorio et al. further teaches that ospemifene can be orally administered in the varying dosage amounts of 5-100 mg/day (which overlaps the recited ranges of 30-90 mg/day of ospemifene; as it relates to claims 10-11 and 19-20) for the treatment of osteoporosis as (i.e., as it relates to claims 7 and 18, see abstract, col. 3, lines 1-10 and 59-64)).

However, DeGregorio et al. does not teach the administration of the drug in connection with intake of foodstuff being taken shortly before, during or shortly after administration (as required by instant claim 1 for example). DeGregorio et al. is also silent of the specific dosages recited by instant claims 11 for example.

Anttila is added to show that structurally similar compounds are known in the art to be administered with or without food.

Antilla teaches administering 60 mg/day of a structurally similar compound



toremifene

Toremifene

administered orally during or after meal

(food) and therefore reasonably meets the limitation of claims 1. The recitation that foodstuff having nutritional value is obvious because all food have nutritional value and therefore would cause secretion of bile acids, and enhance bioavailability of toremifene. Antilla teaches the food is taken following a meal thus shortly after meal and after fasting which reasonable encompasses “during, after or at a certain time interval to meals” (see introduction as required by instant claims 1, see abstract).

Guidance for Industry teaches food effect bioavailability are conducted with new drugs shortly after a meal and compared to fasting condition (see Sec I and II, page 1) wherein Guidance for Industry teaches that food effects are generally greatest when the drug product is administered shortly after a meal is ingested (see page 2, lines 10-16 from the top).

It would have been obvious to one of ordinary skill in the art to expand the teaching of DeGregorio et al to include the teachings of Antilla and administer the drug of DeGregorio at a dosage of 60 mg/day for the treatment of osteoporosis with a

reasonable expectation of success because DeGregorio teaches a dosage range that encompasses the recited range.

Because Antilla teaches a structurally similar compound can be administered with or without food and DeGregorio is silent of food intake with the drug ospemifene, one of ordinary skill in the art would have been motivated to administer DeGregorio's drug with or without food with the expectation of success that the effect will be the same when ospemifene is administered with or without food.

One of ordinary skill in the art would have been motivated to expand Degregorio method of treating osteoporosis with ospemifene to include Antilla dosage amount and teaching of a structurally similar compound administered with or without food to include the teachings of Guidance for Industry for food effect of bioavailability for orally administered drugs with a reasonable expectation of success because Guidance for Industry teaches that drugs should be conducted under fed and fasting conditions wherein under fed conditions the drug can be administered 30 mins after meal (see section E, page 6) and entire teaching). Therefore the administration of ospemifene within one hour, no later than 0.5 hour with food intake is within the purview of the skilled artisan. Thus the teaching of Antilla "that findings may help precision of administration instructions (e.g. administration during or after meals, or at a certain time interval to meals) are well known in the art and are routinely practiced" as taught by Guidance for Industry, the varying point of administering the drug ospemifene (such as 2 hours, one hour, 0.5 hour) after starting the food intake is obvious to be optimized in

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order to find the most effective time interval for administration, as taught by Antilla (see introduction).

Thus the combination of the cited prior art would have been prima facie obvious at the time the claimed invention was filed.

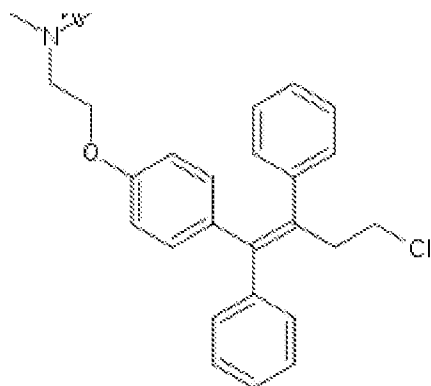
7. Claims 1, 8-9, 12-13, 15-17 and 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Halonen et al. (US 6,245,819) in view of Antilla (1997) and Guidance for Industry (2002).

Halonen teaches administering ospemifene (FC-1271) an estrogen receptor modulator to women suffering from vaginal symptoms (as required by instant claim 9 wherein the drug is administered at a dosage from 30, 60 and 90 (as required by instant claims 12-13, 16-17 and 23-24, see col. 2, lines 60-65). With regards to instant claim 8, Halonen teaches treating vaginal dryness (i.e., mucosal atrophy, see col. 2, lines 29-35).

However Halonen fails to teach treating specifically inhibiting urogenital atrophy as required by instant claim 21 and also fails to teach administration of the drug with a connection of with intake of foodstuff being taken shortly before, during or shortly after administration.

Antilla is added to show that structurally similar compounds are known in the art to be administered with or without food.

Antilla teaches administering 60 mg/day of a structurally similar compound



toremifene

Toremifene

administered orally during or after meal

(food) and therefore reasonably meets the limitation of claims 1. The recitation that foodstuff having nutritional value is obvious because all food have nutritional value and therefore would cause secretion of bile acids, and enhance bioavailability of toremifene. Antilla teaches the food is taken following a meal thus shortly after meal and after fasting which reasonable encompasses “during, after or at a certain time interval to meals” (see introduction as required by instant claims 1, see abstract).

Guidance for Industry teaches food effect bioavailability are conducted with new drugs shortly after a meal and compared to fasting condition (see Sec I and II, page 1) wherein Guidance for Industry teaches that food effects are generally greatest when the drug product is administered shortly after a meal is ingested (see page 2, lines 10-16 from the top).

Even though Halonen did not specifically teach treating urogenital atrophy, in the background section Halonen teaches that during and after menopause elderly women develop symptoms which are due to estrogen deficiency such as vaginal dryness (i.e., mucosal atrophy), urinary incontinence (i.e., urogenital atrophy).

Therefore based on the teaching alone one of ordinary skill in the art would have been motivated to inhibit vaginal atrophy and urogenital atrophy with ospemifene because these disease are estrogen related disorders and reasonable to be treated with an estrogen receptor modulator.

It would have been obvious to one of ordinary skill in the art at the time of filing the instant application to expand the teachings of Halonen to include Antilla's and Guidance for Industry for the treatment of vaginal and urogenital atrophies because Halonen teaches that ospemifene is used for the treatment of such diseases as explained supra.

Based on the teaching of Antilla "that findings may help precision of administration instructions (e.g. administration during or after meals, or at a certain time interval to meals) are well known in the art and are routinely practiced" as taught by Guidance for Industry, the varying point of administering the drug ospemifene (such as 2 hours, one hour, 0.5 hour) after starting the food intake is obvious to be optimized in order to find the most effective time interval for administration, as taught by Anttila (see introduction).

New Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims

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are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-5 and 7-24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of (U.S. Patent No. 6,984,665) in view of Guidance for Industry (2002).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the patented claims recite treating or inhibiting urinary symptoms. Even though the patent is silent to teaching the effect of

food on the drug, Guidance for Industry teaches food effect bioavailability are conducted with new drugs shortly after a meal and compared to fasting condition (see Sec I and II, page 1) wherein Guidance for Industry teaches that food effects are generally greatest when the drug product is administered shortly after a meal is ingested (see page 2, lines 10-16 from the top).

Therefore one of ordinary skill in the art would be motivated to administer food with the drug based on the teaching of Guidance for Industry.

It should be noted that the claims of the patent '665 are drawn to a method for the treatment of urinary symptoms related to urogenital atrophy in women, or to administering effective amounts of formula (I), (i.e., ospemifene).

The '665 patent differs from the claimed invention insofar as it fails to expressly claim a method of enhancing bioavailability. The '665 patent only sets forth a method of treatment or prevention of urinary symptoms related to urogenital atrophy as noted above.

Guidance for Industry teaches food effect bioavailability are conducted with new drugs shortly after a meal and compared to fasting condition (see Sec I and II, page 1) wherein Guidance for Industry teaches that food effects are generally greatest when the drug product is administered shortly after a meal is ingested (see page 2, lines 10-16 from the top).

However, it is contended that a method for treatment skin of atrophy, or epithelial or mucosal atrophy using compound the formula (I), would intrinsically treat

urogenital atrophy, as evidenced by the specification of the '665 patent. For example, the '665 patent defines the symptoms related to urogenital atrophy as urinary and vaginal symptoms (see page3, lines 57-60). Thus, treating a woman with symptoms related to a urogenital atrophy would treat a woman with urinary symptoms when ospemifene is administered with or without food as taught by Guidance for Industry.

9. Claims 1, 3-5 and 7-24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of US 6,245,819 in view of Guidance for Industry.

The instant claims (8 and 15) are drawn to a method of treatment of symptoms related to skin atrophy, or to treating epithelial or mucosal atrophy in women, comprising administering to the woman an effective amount of formula (I) which ospemifene... .

The '819 patent differs from the claimed invention insofar as it fails to expressly claim a method of enhancing bioavailability. The '819 patent only sets forth a method of treatment or prevention of urinary symptoms related to urogenital atrophy as noted above.

However, it is contended that a method for treatment skin of atrophy, or epithelial or mucosal atrophy using compound the formula (I), would inherently treat urogenital atrophy, as evidenced by the specification of the '665 patent. For example, the '665 patent defines the symptoms related to urogenital atrophy as urinary and vaginal symptoms (see page3, lines 57-60). Thus, treating a woman with symptoms

related to a urogenital atrophy would inherently treat a woman with urinary symptoms when ospemifene is administered with or without food. Whether enhanced bioavailability is claimed or not does not change the property of the drug when administered.

10. Claims 1, 3-5 and 7-24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of (U.S. Patent No. 6,984,665) in view of Guidance for Industry (2002).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the patented claims recite treating or inhibiting urinary symptoms. Even though the patent is silent to teaching the effect of food on the drug, Guidance for Industry teaches food effect bioavailability are conducted with new drugs shortly after a meal and compared to fasting condition (see Sec I and II, page 1) wherein Guidance for Industry teaches that food effects are generally greatest when the drug product is administered shortly after a meal is ingested (see page 2, lines 10-16 from the top).

Therefore one of ordinary skill in the art would be motivated to administer food with the drug based on the teaching of Guidance for Industry.

It should be noted that the claims of the patent '665 are drawn to a method for the treatment of urinary symptoms related to urogenital atrophy in women, or to administering effective amounts of formula (I), (i.e., ospemifene).

The '665 patent differs from the claimed invention insofar as it fails to expressly claim a method of enhancing bioavailability. The '665 patent only sets forth a method of treatment or prevention of urinary symptoms related to urogenital atrophy as noted above.

Guidance for Industry teaches food effect bioavailability are conducted with new drugs shortly after a meal and compared to fasting condition (see Sec I and II, page 1) wherein Guidance for Industry teaches that food effects are generally greatest when the drug product is administered shortly after a meal is ingested (see page 2, lines 10-16 from the top).

However, it is contended that a method for treatment skin of atrophy, or epithelial or mucosal atrophy using compound the formula (I), would intrinsically treat urogenital atrophy, as evidenced by the specification of the '665 patent. For example, the '665 patent defines the symptoms related to urogenital atrophy as urinary and vaginal symptoms (see page3, lines 57-60). Thus, treating a woman with symptoms related to a urogenital atrophy would treat a woman with urinary symptoms when ospemifene is administered with or without food as taught by Guidance for Industry.

Affidavit

11. The affidavit submitted by Risto Lammintausta under 37 CFR 1.132 filed 4/30/10 is insufficient to overcome the rejection of claims 1, 3-5 and 7-24 based upon the rejection under 35 USC 103 as set forth in the this action because:

Appellant argues that "Ospemifene is a selective estrogen receptor modulator or a "SERM." A SERM, by definition, displays estrogenicity in at least some tissues (i.e., agonism), but may have no estrogen effect in other tissues, and may in fact block estrogen action in some tissues (i.e. antagonism). (Burger HG: Selective Estrogen Receptor Modulators. Horm.Res.2000;53 Suppl 3:25-29)" and also states that "Current evidence suggests that the pharmacology of SERMs with respect to their estrogen-mediated effects is potentially unique to each member of the class".

Appellant further argues that "Contrary to the Examiner's assertions, Anttila does not disclose administering a metabolite of toremifene. Anttila discloses administering 60 mg tablets of toremifene. Anttila does measure the blood levels of a major metabolite of toremifene, namely N-demethyltoremifene (or desmethyltoremifene), but no metabolite was administered".

That "[t]he Examiner is also incorrect in his assertion that food would inherently enhance the bioavailability of toremifene. The Anttila reference teaches that toremifene "works equally well with or without administration of food" and "The DeGregorio et al. reference relates to the use of ospemifene to treat or prevent osteoporosis. The DeGregorio et al, reference does not teach the administration of a drug with a meal nor does it teach the use of ospemifene to treat either vaginal atrophy or symptoms thereof"

In response to Appellant's argument that ospemifene is a selective estrogen receptor modulator or a "SERM." A SERM, by definition, displays estrogenicity in at least some tissues (i.e., agonism), but may have no estrogen effect in other tissues is not the issue here, the claims do not require that the drug ospemifene displays estrogenicity. The

claims recite a method of enhancing the bioavailability which does not affect its selectivity to specific organs. When the drug is enhanced it will still maintain its specificity.

Based on Guidance for Industry which teaches food effect bioavailability are conducted with new drugs shortly after a meal and compared to fasting condition (see Sec I and II, page 1) it has clearly showed that every drug undergoes how food affects administration and then prescribed accordingly.

In summary

As discussed above DeGregorio et al. teaches ospemifene (see abstract), as required by instant claims 1-2, 7, 10-11, 14 in a pharmaceutically acceptable salt is obvious since it is in a pharmaceutical composition. DeGregorio et al. further teaches administering orally 5-100 mg/day of ospemifene (as it relates to claims 10-11 and 19-20) for the treatment of osteoporosis as (i.e., as it relates to claims 7 and 18, see abstract, col. 3, lines 1-10 and 59-64)).

Antilla teaches administering toremifene at a dose of 60 mg a day (structurally similar to ospemifene) with food or without food. Guidance for Industry teaches food effect bioavailability are conducted with new drugs shortly after a meal and compared to fasting condition (see Sec I and II, page 1) wherein Guidance for Industry teaches that food effects are generally greatest when the drug product is administered shortly after a meal is ingested (see page 2, lines 10-16 from the top).

12. No claim is allowed.

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13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, BRANDON FETTEROLF can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/S. V. G./
Examiner, Art Unit 1618
1/11/11

/Brandon J Fetterolf/
Supervisory Patent Examiner, Art Unit 1628